510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k041927

B. Purpose for Submission:

Clearance of new device

C. Measurand:

Low Density Lipoprotein (LDL)

D. Type of Test:

Quantitative Colorimetric Assay

E. Applicant:

Diagnostic Chemicals Limited

F. Proprietary and Established Names:

LDL-Advance Assay

G. Regulatory Information:

1. Regulation section:
   21 CFR §862.1475, Lipoprotein test system

2. Classification:
   Class I, meets limitations of exemptions 21 CFR 862.9 (c)(4)

3. Product code:
   MRR, system, test, low density lipoprotein

4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   For the quantitative determination of low density lipoprotein fractions of cholesterol in serum.

A lipoprotein test system is a device intended to measure lipoprotein in serum. Low Density Lipoprotein (LDL) cholesterol measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

2. Indication(s) for use:

   Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

3. Special conditions for use statement(s):

   This assay has not been tested or certified by the CRMLN.

   For in vitro diagnostic use.

   For professional use only.

4. Special instrument requirements:

   Hitachi 717 and 917 Analyzers

I. Device Description:

The LDL-Advance Assay contains two wet reagents and an assay calibrator (for information on the calibrator, see k041926).

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche LDL-C Plus2nd Generation Assay

2. Predicate 510(k) number(s):
   k982848

3. Comparison with predicate:

   The device and its predicate share the same intended use and reaction principle. There are no major differences between the device and its predicate in design, or function.

K. Standard/Guidance Document Referenced (if applicable):

NCCLS Guideline EP5, Evaluation of Precision performance of Clinical Chemistry Devices

NCCLS Guideline EP6, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach
NCCLS Guideline EP-7, Interference testing in Clinical Chemistry

L. Test Principle:

The serum sample is mixed with the two reagents, and lipoproteins in the sample other than LDL are selectively bound by a combination of phosphorus compounds and detergents. The LDL cholesterol in the sample initiates the following reaction [HDAOS = N(2-hydroxy-3-sulfopropyl)-3,5-dimethylaniline]:

$$\text{LDL-Cholesterol} \xrightarrow[\text{Cholesterol esterase}]{\text{------>}} \text{Cholesterol + fatty acid}$$

$$\text{Cholesterol + } O_2 \xrightarrow[\text{Cholesterol Oxidase}]{\text{------>}} \Delta\text{4-Cholestenon + } H_2O_2$$

$$2H_2O_2 + \text{4-amino-antipyrine + HDAOS} \xrightarrow[\text{Peroxidase}]{\text{------>}} \text{Quinone pigment + } 4H_2O$$

The color intensity produced by the reaction is measured spectrophotometrically at 600 nm and is directly proportional to the concentration of LDL cholesterol in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

The imprecision of the device was evaluated according to NCCLS guideline EP5-A. Three levels material were assayed in duplicate twice per day for 20 dys (total n = 80). Results are summarized below (units = mg/dL):

		Within run		**Between run**		**Total**	
	Mean	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**
Level 1	77.59	1.07	1.4 %	2.89	3.8 %	3.12	4.1 %
Level 2	152.68	1.55	1.0 %	6.15	4.0 %	6.35	4.1 %
Level 3	290.79	3.53	1.2 %	4.33	1.5 %	7.37	2.5 %

b. Linearity/assay reportable range:

The reportable range of the assay is 1-400 mg/dL (0.03 – 10.4 mmol/L).

Linearity was evaluated by spiking a human serum pool with under-reconstituted control material and making serial dilutions with saline to achieve the following theoretical concentrations: 413.465, 271.647, 217.069, 151.742, 86.001, and 20.673 mg/dL. The

theoretical concentration was compared to the observed concentration and the following least squares regression statistics were observed: Observed = 1.012(Theroetical) + 0.116. The device is linear from 20.673 to 400 mg/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

For information on the included calibrator, please see k041926.

d. Detection limit:

The analytical sensitivity was determined by adding three standard deviations to the mean of 10 replicate measurements of saline. This value was determined to be 0.363 mg/dL.

e. Analytical specificity:

The assay was evaluated for potential interference from hemoglobin, bilirubin, and lipemia. Hemoglobin up to 1000 mg/dL and bilirubin up to 40 mg/dL caused < 10% interference. Intralipid levels up to 100 mg/dL (equivalent to triglyceride levels up to 300 mg/dL) caused < 10% interference.

The sponsor provides references to common drug interferences in clinical chemistry tests.

f. Assay cut-off:
Not applicable

2. Comparison studies:
   a. Method comparison with predicate device:

Forty patient serum samples were assayed using the device and the predicate assay. The results were compared and the resulting Deming and Least squares regression statistics are as follows (units = mg/dL):

Least Squares: (Device) = 0.999(Predicate) – 4.851
R = 0.9971
Slope (95% CI): 0.999 (0.974 – 1.024)
Intercept (95% CI): -4.851 (-9.703 – 0.001)
Std Err Est: 5.624

Deming: (Device) = 1.002(Predicate) – 5.376
Slope (95% CI): 1.002 (0.977 – 1.027)
Intercept (95% CI): -5.376 (-10.232 – -0.521)
Std Err Est: 5.628

b. Matrix comparison:

Not applicable

3. Clinical studies:
   a. *Clinical Sensitivity:*
      Not applicable

   b. *Clinical specificity:*
      Not applicable

   c. Other clinical supportive data (when a. and b. are not applicable):
      Not applicable

4. Clinical cut-off:
   Not applicable

5. Expected values/Reference range:

The sponsor cites the National Cholesterol Education Program Adult treatment Panel III for the following reference ranges:

	Desirable	**Borderline High Risk for CHD**	**High Risk for CHD**	**Very High Risk for CHD**
LDL Cholesterol (mg/dL)	< 100	130 – 159	160 – 180	≥ 190

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.